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TITLE: Integrated Eye Tracking and Neural Monitoring for Enhanced Assessment of mild TBI

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14. ABSTRACT During the Year 3 POP (08 MAR 2015 – 07 MAR 2016), data collection for the pilot study (n=30) was completed. HRPO approval for the primary study was received and data collection commenced. To date, 27 participants have been enrolled in the primary study. Continued recruitment efforts, including initiation of collaborative efforts with the Center for Neuroscience and Regenerative Medicine (CNRM), have helped to increase enrollment in the second half of Year 3. Administrative and technical delays were encountered at the National Intrepid Center of Excellence (NICoE), but these delays are nearing resolution and we anticipate the initiation of the neuroimaging portion of the study early in Year 3. The fMRI task has been completed and is in beta testing. Key milestones are behind schedule by approximately 4 quarters, but we are attempting to make up time through accelerated recruitment efforts and data collection for the primary study.					
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Introduction

The objective of this project is to validate a combined EEG and eye tracking system aimed at assessing compromised cognitive function stemming from mild traumatic brain injury (mild TBI). Research suggests that the neural injuries resulting from mild TBI do not always produce observable performance deficits. However, subjective ratings suggest that the level of effort required to perform at a given level can be higher with mild TBI; associated neuroimaging data reveal a broader recruitment of cortical neurons to accomplish tasks in mild TBI relative to uninjured individuals [1-3]. The research described here combines information from two distinct physiological sensing approaches to make inferences about injury-related changes in cognitive function using measures that are sensitive to cognitive effort. The goal is to combine the expertise of academic, military, and industry researchers to create a practical and effective neurodiagnostic assessment tool that can be used in a broad range of contexts in which cognitive assessment is relevant. Validation of the integrated EEG and eye tracking system will include evaluation of the specificity and sensitivity of these measures based on characterizations of injury severity, performance on a neurocognitive test battery, and self-report measures of cognitive efficacy. We will also include functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) to characterize the extent of functional cortical recruitment and white matter injury, respectively. The inclusion of fMRI and DTI will provide an objective basis for cross-validating the EEG and eye tracking system. Both the EEG and eye tracking data will be collected in the context of a dual-task experimental paradigm with visual target detection.

Keywords

TBI, concussion, saccadic, eye tracking, EEG, cognition

Overall Project Summary

During the Year 3 period of performance (03/08/2015 – 03/07/2016), significant progress was made in the overall research effort. Enrollment for the pilot study was completed and closure documents for the pilot study were submitted and approved by USU #1 and HRPO. To date, 30 participants have been enrolled in the pilot study and 27 participants have been enrolled in the primary study. Recruitment efforts are under way to bolster the pace of enrollment. Following resolution of administrative and technical delays at the National Intrepid Center of Excellence (NICoE), we are in the process of initiating the neuroimaging portion of the study. The fMRI task is complete and currently in beta testing. The contracting process is under way for Y4 Q2 software development related to the optimization phase of the research effort. Key milestones are approximately 4 quarters behind schedule due to delays in initial contract/subaward negotiations and transition to a new laboratory location. The statement of work was recently revised to reflect the updated schedule. Please note that some carry-forward funds will be used to complete tasks initially scheduled for Year 3 but now scheduled for Year 4, in order to preserve funds for a 1-year no-cost extension (request to be submitted).

Progress related to specific milestones as outlined in the statement of work is outlined below:

Obtain IRB approvals for Study #1 (Primary). Initial approval for the primary study was received from USU IRB #1 on January 12, 2015 from HRPO on March 27, 2015. The continuing review was submitted and approved by USU IRB #1 on 10/08/2015 and by HRPO on 1/27/2016.

Begin enrollment for Study #1 (Primary). As of the end of Year 3 POP, 27 participants have been enrolled in the primary study (Controls: n = 11; Mild TBI: n = 10; Moderate – Severe: n = 6).

Continued development of the recruitment plan during this POP has been a primary focus of the study team. Collaboration with the Center for Neuroscience and Regenerative Medicine (CNRM) was approved by USU IRB #1 on 22/DEC/2015. The CNRM recruitment core enrolls participants into one of two screening protocols (military or civilian) and then refers participants based upon eligibility to CNRM funded and collaborative studies. Study personnel have been working with members of the recruitment core to process and screen referrals eligible for this research effort. Additionally, team members have attended meetings of various organizations, including Serving Together and the Family Plus Collaborative, to learn about local outreach events that are intended to provide service members with information and resources that promote mental, physical, and emotional well-being. As a result of attending these meetings, study personnel learned of and represented the Ettenhofer Laboratory for Neurocognitive Research at the Brain Injury Awareness Resource Fair at the Walter Reed National Military Medical Center (WRNMMC) in March 2016. Along with other organizations, team members will attend the Fifth Annual Youth Health and Fitness Fair in April 2016 to discuss this research effort with interested patrons. Advertisements have been posted at USUHS, gym and eating facilities at WRNMMC, University of Maryland, College Park (UMCP), and various TBI and rehabilitation clinics. Advertisements have also been sent out electronically via the WRNMMC Intranet, and various list serves at NIH and UMCP. The study team conducts biweekly recruitment meetings to regularly track the success of our current recruitment efforts and brainstorm new sources of recruitment.

Update DOD/TATRC representatives on progress at annual meeting. Dr. Ettenhofer attended the Military Operational Medicine Research Program (MOMRP) meeting at Fort Detrick, MD from July 29 – July 30, 2016. Progress updates were provided to DOD/TATRC representatives and revisions to the protocol were implemented based upon feedback received at this meeting.

Begin preliminary data analyses for Study #1 (Primary). Preliminary data analyses for the primary study are under way. Study personnel are working to refine the data processing pipeline to ensure data included in analyses are high quality. Planned analyses include assessing differences in behavioral (manual and saccadic) performance and psychophysiological responses between-groups (Controls, Mild TBI, and Moderate-Severe TBI participants) and within-subjects on the custom cognitive tasks (Fusion N-Back, Fusion Color Match, and Fusion Coastal Drive). Primary variables of interest include saccadic latency, saccadic duration, saccadic reaction time, manual reaction time, pupillary response, and several EEG/ERP components. Based on results from the pilot study, we expect to see an overall effect of cognitive workload and trial type within-subjects (decreased performance and altered psychophysiological responses as task difficulty increases) in all groups. Additionally, we expect that TBI groups will have significantly degraded performance and psychophysiological response compared to controls, particularly for more challenging task components.

Disseminate project plans and progress.

See *Publications, Abstracts, and Presentations* below for information about progress in disseminating project methods, plans and progress.

Key Research Accomplishments for this Year

- Completed data collection for the pilot study
- Initiated data collection for the primary study
- Developed enhanced participant recruitment pipeline
- Initiated contracting services for software development related to the optimization phase of the research effort.

Conclusions

The primary goal of the Fusion project is to develop and validate methods for evaluating changes in behavioral performance, saccadic performance, and brain activation that occur at different levels of cognitive load. It is expected that individuals with poorer cognitive efficacy resulting from TBI will demonstrate more significant performance trade-offs and greater increases in brain activation with increasing load. Preliminary analyses suggest that the Fusion tasks used for integrated eye tracking and neural monitoring are able to successfully discriminate cognitive workload across difficulty levels. This provides a promising basis for the extraction of valuable data relevant to detecting changes in cognitive efficacy after TBI. Ongoing research will evaluate the Fusion tasks for this purpose, and examine potential mechanism of any effects observed.

Publications, Abstracts, and Presentations

The following manuscript, describing scientific methods and results from the pilot study of this project, has been published during the Year 3 POP:

Safford, A., Kegel, J., Hershaw, J., Girard, D., & Ettenhofer, M. (2015). Eye-Tracking Technology for Estimation of Cognitive Load After Traumatic Brain Injury. In *Foundations of Augmented Cognition* (pp. 136-143). Springer International Publishing.

The following presentation disseminated scientific methods and results from the pilot study of this research effort:

Safford, A., Kegel, J., Hershaw, J., Girard, D., & Ettenhofer, M.L. (August, 2015). *Eye-movement Based Detection of Subtle Cognitive Impairment for Enhanced Assessment of Mild Traumatic Brain Injury*. Paper presented at the 17th Annual Conference on Human-Computer Interaction, Los Angeles, CA. Conference proceedings published in *Lecture Notes in Computer Science*.

The following invited colloquia, given by Dr. Ettenhofer during the project period, have included dissemination of scientific methods and results of this study:

Ettenhofer, M.L. (March, 2015). "Novel Technologies for Assessment and Rehabilitation of Traumatic Brain Injury." Brain Injury Awareness Seminar, Walter Reed National Military Medical Center.

Ettenhofer, M.L. (April, 2015). "Cognitive Assessment and Intervention for Mild TBI." Department of Medical and Clinical Psychology, Uniformed Services University.

Ettenhofer, M.L. (January, 2016). "Development and Evaluation of Neurocognitive Eye Tracking." Center of Excellence for Stress and Mental Health, VA San Diego Health Care System.

Ettenhofer, M.L. (March, 2016). "Neuroscientific Applications of Cognitive Eye Tracking." Neuroscience Group, University of California, San Diego.

Inventions, Patents, and Licenses

None to report.

Reportable Outcomes

Nothing to report.

Other Achievements

Nothing to report.

References

1. McAllister, T.W., et al., *Differential working memory load effects after mild traumatic brain injury*. Neuroimage, 2001. **14**(5): p. 1004-12.
2. Chen, J.K., et al., *Functional abnormalities in symptomatic concussed athletes: an fMRI study*. Neuroimage, 2004. **22**(1): p. 68-82.
3. McAllister, T., et al., *Brain activation during working memory 1 month after mild traumatic brain injury: a functional MRI study*. Neurology, 1999. **53**(6): p. 1300-8.

Appendices

There are no appendices for this report.

Supporting Data

Please see the following publication for data relevant to this report:

Safford, A., Kegel, J., Hershaw, J., Girard, D., & Ettenhofer, M. (2015). Eye-Tracking Technology for Estimation of Cognitive Load After Traumatic Brain Injury. In *Foundations of Augmented Cognition* (pp. 136-143). Springer International Publishing.